Serial No.	09/810,988
Applicant:	Gerhard Scheuch *et al.*
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Title:	DEVICE FOR THE CONTROLLED INHALATION OF THERAPEUTIC AEROSOLS
Art Unit:	3731
Examiner:	Glenn K. Dawson
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DECLARATION UNDER 37 CFR § 1.132

In response to the Office Action dated February 20, 2008, I, Bernhard Muellinger, do hereby declare and say as follows:

BACKGROUND INFORMATION

1. I am a co-inventor of the present application.

2. I obtained a degree in Precision and Micromechanical Engineering in 1995 from the University of Applied Science in Munich, with a focus on medical device technology.

3. From 1995 to 1998, I was employed at the GSF – Research Centre for Environment and Health, working on the research project "Optimization of Aerosol Deposition with Monodisperse Encapsulated Particles". I held different positions related to aerosol research while I was at GSF.

4. From 1998 to 2000, I was employed at the Asklepios Clinics in cooperation with the Clinical Research Group of GSF and developed new pulmonary diagnostic technologies and performed clinical trials in aerosol delivery research.

5. Since 2000, I have been employed at Activaero GmbH. I am currently the Vice President of Device & Clinical Development, and I am responsible for medical device development and clinical development. I have managed numerous projects developing products including the AKITA® inhalation system, the AKITA²™ inhalation system, the AKITA JET™ inhalation system and several customer specific medical devices. I am also responsible for optimization of pharmaceutical formulations, dosing and aerosol targeting strategies in preclinical and clinical drug development projects within Activaero GmbH. I have extensive experience in clinical trials in drug delivery by aerosols.

THE APPLICATION

6. I have read and understood the above referenced patent application, including the specification, claims and the relevant prior art.

7. The standard I used for anticipation is whether every element of a claim is disclosed in a single prior art reference.

8. The standard I used for obviousness is whether the claims would have been obvious to an ordinary person skilled in the art in light of the references cited.

9. The Examiner rejected independent claims 25, 43, and 44 as being anticipated by Brooker (6,269,810).

10. Brooker discloses "a pulmonary dosing system and method for supplying to a patient a predetermined amount of respirable therapeutically active material" (Abstract).

11. The control system in Brooker operates "the pulmonary dosing system in accordance with operator inputs selecting the number of patient exhales between pulses, the pulse length, and the amount of material to be dispended to the patient" (column 2, lines 55-59).

12. Brooker focuses on an exhaust port connected to an exhalation line, and a filter that captures the exhaled aerosol.

13. Brooker specifically states that its apparatus "does not include a respirator or the like, and is intended for use with patients who can breathe normally" (column 4, lines 33-35).

14. Brooker's device does not adjust respiratory flow or tidal volume. Instead, similar to every other prior art inhalation device, a patient using Brooker's device would be told and trained to inhale deeply. "With cooperation from the patient (in drawing a deep breath), the device enables this deep penetration by providing that the metered volume of drug aerosol from the plenum forms the first part of each inhaled breath...." (column 6, lines 17-21). The volume of the inhaled breath is not metered; the volume of the drug aerosol is set by an internal plenum to give an aerosol pulse.

15. Brooker states that the aerosol pulse should be adjusted to the tidal volume and vital capacity. Then the aerosol pulse can be programmed into the control system. The pulse is adjusted, not the respiratory flow or tidal volume. "For the more efficient operation, the plenum is provided during the exhalation phase with a drug aerosol volume equal to about 1/4 to 1/2 of the patient's normal inspired volume" (column 6, lines 42-45).

16. Additionally, it is clear from Brooker that there is no further control besides control of an aerosol pulse. In fact, there is a lack of control, and the tidal volume is not controlled by the system. "The tidal volume and vital capacity may be determined by known pulmonary function tests. The control system is then programmed to deliver the selected amount of drug aerosol to the plenum based on the pulmonary function of the animal or human" (column 6, lines 47-51).

17. Respiratory flow and tidal volume are not adjusted in Brooker. Even when patients are guided, they do not inhale with the optimum flow rate and inhalation volume. In fact, studies have shown that breathing patterns can not be effectively controlled by training patients to breathe, as explained in the attached publication by Köhler et al. (Journal of Aerosol Medicine, 2005, submitted in the IDS dated July 11, 2006).

18. Therefore, Brooker could not control the application of a pharmaceutical aerosol to provide an accurate dosage.

19. Brooker does not disclose individually adjusting an inhalation device to the patient to be treated by adapting a dosage of at least one aerosol on the basis of the inhalation parameters. More specifically, Brooker does not disclose adjusting flow rate or tidal volume using individual patient parameters or aerosol parameters. Therefore, claims 25, 43, and 44 are not anticipated by Brooker.

20. The Examiner rejected independent claims 25, 43, and 44 as being obvious over Brand (6,606,989) in view of Brooker.

21. As discussed above, Brooker does not teach or suggest individually adjusting an inhalation device to the patient to be treated by adapting a dosage of at least one aerosol on the basis of the inhalation parameters, nor does Brooker teach or suggest adjusting flow rate or tidal volume based on inhalation parameters.

22. Brand teaches "a device for deposition of a medicament in a liquid form in the lungs" (claim 1, column 4, lines 33-34). Brand uses a pre-settable volumetric flow of compressed air and flow rate that can be set "over a range from 0 to 1000 cm^3/s" (column 3, lines 39-40).

23. Brand also teaches that "setting the operating pressure of the vaporizer, for instance over a range of values from 0 to 2 bar" (column 3, lines 49-50) is possible. Timing parameters are also set. "The inhaled volume then derives from the inhalation period and the flow of inhalation" (column 4, lines 6-8). The inhalation period can be set from 0 to 20 seconds.

24. Even well trained pulmonologists are not familiar with the scientific background of aerosol particle deposition within the lungs. Offering such a broad range of inhalation parameters that can be set by the physician and the patient prevents optimum therapy for an individual patient.

25. Even after extensive breathing training, patients typically revert to a respiratory flow rate and tidal volume that are comfortable to them. In clinical trials with conventional inhalation devices, it was shown that the incorrect breathing pattern is one of the most important errors that is made during inhalation treatment. (Giraud et al. 2002, 19:246-251, European Respiratory Journal, copy attached).

26. The Giraud reference specifically states that misuse of pressurized metered-dose inhalers is mainly due to poor coordination (see Abstract).

27. The Giraud reference also states that "there was no significant direct relationship between education and AIS, which is most likely due to the fact that education is not always successful (errors are corrected in only 50% of poor users, 50% of whom return to their 'bad habits' within a few weeks)...." (page 250).

28. The Giraud reference also states that "[the] use of devices which alleviate coordination problems should be reinforced in pressurized metered-dose inhaler misusers." (Abstract) and "[u]se of devices that make inhalation technique easier... should be reinforced in pressurized metered-dose inhaler misusers" (page 250). The present invention makes the inhalation technique much easier, since the user no longer needs to be "coordinated" and breath correctly.

29. Controlled aerosol delivery to the lungs can only be guaranteed when inhalation parameters are inputted into the inhalation device, as claimed in claims 25, 43 and 44.

30. Brand does not teach or suggest individually adjusting an inhalation device to the patient to be treated by adapting a dosage of at least one aerosol on the basis of the inhalation parameters and Brand does not teach or suggest adjusting flow rate or tidal volume based on inhalation parameters. Therefore Brand does not teach the elements in claims 25, 43, and 44 missing from Brooker.

31. Servidio (5,598,838) teaches an "improved pressure support ventilatory assist system for providing pressurized air to a patient by way of a nasal mask" (column 2, lines 35-38).

32. Servidio's invention is a ventilator, which is in a completely different field than the inhalation device of the present invention.

33. Servidio does not teach or suggest control of an inhalation device for inhalation of aerosols. Servidio does not teach or suggest individually adjusting an inhalation device to a patient to be treated by adapting a dosage of at least one aerosol on the basis of the inhalation parameters. Servidio also does not teach or suggest adjusting flow rate or tidal volume based

on the inhalation parameters. Instead, Servidio teaches a pressure support device to provide air under positive pressure.

34. Therefore, Servidio does not teach the elements in claims 25, 43, and 44 missing from Brand and Brooker.

35. Willemot (5,560,353) teaches "a system [that] supplies discrete puffs of gas, containing particles of an active product, to a patient's respiratory tract" (Abstract). Willemot teaches a "device for controlling the supply of doses of carrier gas from source 3 including a three way valve 5 coupled to a sensor 6 which is responsive to the phases of inhalation and exhalation of the user" (column 2, lines 9-13).

36. Neither respiratory flow nor tidal volume is adjusted by the device taught in Willemot. Willemot only supplies gas flow for driving the nebulizer. The inhalation flow rate is not controlled by the device.

37. Willemot's device only provides "gas flow control [that] delivers a metered amount of the gas to the nebulizer and to the user in each puff" (Abstract). As described in the Figure, only the nebulizer nozzle is supplied over tubing (2) and the patient can also inspire through the additional air inlet (4).

38. Willemot does not teach or suggest individually adjusting an inhalation device to a patient to be treated by adapting a dosage of at least one aerosol on the basis of the inhalation parameters and Willemot does not teach or suggest adjusting flow rate or tidal volume based on inhalation parameters. Therefore, Willemot does not teach the elements in claims 25, 43, and 44 missing from Brooker and Brand.

CONCLUSION

Based on the above analysis, I conclude that the claims in the present patent application are not anticipated by Brooker or obvious over any combination of the references cited.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are

punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: July 17, 2008 By: B. Muellinger
Bernhard Muellinger